UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,887	07/11/2000	Kirk Hogan	HOGAN-04448	9983

72960 7590 02/22/2011

Casimir Jones, S.C.
2275 DEMING WAY, SUITE 310
MIDDLETON, WI 53562

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
02/22/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte KIRK HOGAN

Appeal 2010-006503
Application 09/613,887
Technology Center 1600

Before ERIC GRIMES, LORA M. GREEN, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a method of screening patients for risk of surgical complications. The Examiner has

---

[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

This application was the subject of an earlier appeal (Appeal 2006-1560, decided July 25, 2006). Appellant resumed prosecution and amended the claims. The Examiner rejected the amended claims and this appeal followed.

Claims 106-125 and 127-191 are on appeal. Claim 106 is representative and reads as follows:

106. A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and

b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile;

c) selecting a perioperative course of action based on information from said genomic profile, wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure, thereby determining a risk for complications during said surgical procedure; and

d) performing said surgical procedure wherein said perioperative course of action is used by at least one of the group consisting of an anesthesiologist, a nurse, and a surgeon.

I.

The Examiner has rejected claims 106-124, 127-133, 135-150, 161-186, 189, and 191 based on Miller,[2] either of Quane[3] or AAS,[4] either of La Du[5] or Pharmacogenetics,[6] either of Evans[7] or Poort,[8] Hoon,[9] and Hacia[10] (Answer 3-4).

The rejection now on appeal is based on the same evidence as the rejection appealed in 2006-1560 (2006-1560 Opinion, page 5). We incorporate our previous fact-finding regarding the scope and content of the prior art (2006-1560 Opinion, pages 7-10). In the previous appeal, we

---

[2] Ronald D. Miller (ed.), ANESTHESIA, VOL. 2, Churchill Livingstone, NY, 1323-1333 (1981).
[3] Kathleen A. Quane et al., *Detection of a novel common mutation in the ryanodine receptor gene in malignant hyperthermia: implications for diagnosis and heterogeneity studies,* 3 HUMAN MOLECULAR GENETICS, 471-476 (1994).
[4] B. N. La Du, *Butyrylcholinesterase variants and the new methods of molecular biology,* 39 ACTA ANAESTHESIOLOGICA SCANDINAVICA, 139-141 (1995).
[5] Bert N. La Du et al., *Proposed nomenclature for human butyrylcholinesterase genetic variants identified by DNA sequencing,* 11 CELLULAR AND MOLECULAR NEUROBIOLOGY, 79-89 (1991).
[6] The reference is cited as *"Pharmacogen[e]tics, Chapter 4, 309-326"* in the Information Disclosure Statement received April 6, 2001 (reference number 202 in the IDS).
[7] William E. Evans et al., *Pharmacogenomics: Translating functional genomics into rational therapeutics,* 286 SCIENCE, 487-491 (1999).
[8] Poort et al., *A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis,* 88 BLOOD, 3698-3703 (1996).
[9] Hoon et al., U.S. Patent 6,057,105, issued May 2, 2000.
[10] Hacia, *Resequencing and mutational analysis using oligonucleotide microarrays,* 21 NATURE GENETICS SUPPLEMENT, 42-47 (1999).

concluded that the disclosures of Quane, Pharmacogenetics, AAS, Evans, and Hacia,

> viewed collectively by a person of ordinary skill in the art, would have made obvious the method defined by claim 74. That is, it would have been obvious to a person of skill in the art to test a patient who was scheduled for surgery to determine whether the patient had any of the genetic polymorphisms known to be associated with specific surgery- or anesthesia-related complications, including the RYR1 mutations discussed by Quane, the BChE mutations discussed by AAS, and the CYP2D6 mutations discussed by Pharmacogenetics. The skilled artisan would have found it obvious to conduct such testing (using, for example, DNA hybridization techniques such as those disclosed by Evans and Hacia) in order to avoid the known risk of side-effects, including death, that were likely to occur when patients having a particular genetic make-up were given particular drugs.

(*Id.* at 10-11, footnote omitted.) We adhere to our previous conclusion.

Claim 106, currently on appeal, adds two limitations to the claim addressed in 2006-1560: "selecting a perioperative course of action based on information from said genomic profile," and "performing said surgical procedure wherein said perioperative course of action is used by at least one of the group consisting of an anesthesiologist, a nurse, and a surgeon."

The issue therefore is whether the prior art references cited by the Examiner would also have made obvious the steps recited in claim 106 that were not included in the previously claimed method. The Examiner concluded that:

> The ordinary artisan would have . . . taken the results from the genetic tests and selected a perioperative course of action that was consistent with the results obtained from the genetic marker information. Moreover, once the selection was completed, the medical professionals would have performed the

> surgical procedure according to these directions to ensure the safety of the patient.

(Answer 10.)

We agree with the Examiner's reasoning. As we concluded in the previous appeal, testing for genetic polymorphisms known to be associated with specific surgery- or anesthesia-related complications would have been obvious "in order to avoid the known risk of side-effects, including death, that were likely to occur when patients having a particular genetic make-up were given particular drugs" (2006-1560 Opinion, page 11). That result would only be obtained if, as recited in claim 106, the perioperative course of action was selected based on the results of the testing (the genomic profile), and the perioperative course of action was then used in the surgical procedure. The additional limitations of claim 106 therefore would have been obvious based on the cited references.

Appellant argues that the appropriate person of ordinary skill in the art is an anesthesiologist, and "ordinary anesthesiologists or other perioperative clinicians were not familiar with, and would not and did not look to the Office's non-analogous molecular biology references" (Appeal Br. 21; see also Reply Br. 5). Appellant cites the Second Hogan Declaration[11] and the Coursin Declaration[12] as evidence that, at the time the invention was made, clinicians did not carry out genetic testing prior to surgery despite a desire to detect risks for complications (Appeal Br. 22-23). Appellant also cites the Coursin Declaration as evidence that those skilled in the art would not have

---

[11] Declaration under 37 C.F.R. § 1.132 of Kirk Hogan, filed July 8, 2002.
[12] Declaration under 37 C.F.R. § 1.132 of Douglas Baird Coursin, filed June 11, 2007.

considered it obvious to combine the disclosures of the cited references (*id.* at 25-27).

These arguments are not persuasive. The evidence of record supports the Examiner's conclusion that an anesthesiologist of ordinary skill would have considered it obvious to test for the presence of genetic markers that were known to be associated with a risk of complications during anesthesia. For example, Quane states that "[t]he mutation reported here . . . should be of significant value for MHS [malignant hyperthermia susceptible] diagnosis by genetic means" (Quane 474, left col.). The authors of Quane were employed by several European hospitals and therefore reasonably appear to be clinicians (*id.* at 471). Similarly, the author of AAS, who was from the Departments of Anesthesiology and Pharmacology at the University of Michigan Medical School (AAS 141, right col.), stated that the "principles of molecular biology tests and their application to BChE variants are well illustrated . . . , and anesthesiologists need to keep up to date about these applications" (*id.* at 140-141). The author also states that, since succinylcholine and mivacurium are "potentially toxic in people with a BChE deficiency, it is worth keeping a record of the individuals carrying such genetic traits" (*id.* at 139, left col.).

The fact that, as testified by Dr. Hogan and Dr. Coursin, those skilled in the art did not actually carry out pre-surgery genetic testing (Appeal Br. 22, 25-27), does not establish that doing so would not have been obvious under the standard of 35 U.S.C. § 103. As discussed in Appeal 2006-1560 (pages 13-14), the First Hogan Declaration provides evidence that the standard of care in anesthesia was determined based, at least in part, on cost-

effectiveness. Obviousness under § 103, however, is based on technological compatibility, not economics. *See In re Farrenkopf*, 713 F.2d 714, 718 (Fed. Cir. 1983). The method suggested by the prior art therefore would have been obvious under the appropriate standard, even if it would have cost too much to carry out such testing routinely.

Appellant also argues that the cited references are missing various elements of certain claims on appeal (Appeal Br. 32-49; Reply Br. 6-8).

The Examiner, however, has provided a reasoned basis for concluding that these elements, even if not expressly disclosed in the cited references, would nonetheless have been obvious to a person of ordinary skill in the art (Answer 10-13). Appellant has not provided an adequate basis for concluding that the disputed limitations would not have been obvious. The fact that they are not explicitly disclosed in the prior art is not an adequate basis for concluding that they would not have been obvious. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("[T]he analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.").

Appellant also argues that the Examiner erred in determining the difference between the prior art and claims 143, 160, and 186 (Appeal Br. 49). Appellant does not, however, provide any basis for concluding that any fact-finding errors made by the Examiner led to an erroneous conclusion of obviousness. Appellant's argument therefore does not persuade us that the rejection of these claims should be reversed.

Finally, Appellant argues that "the Office has not examined independent claims 143 or 144, or claims dependent thereupon. Nowhere in the rejections are the elements of these claims addressed." (Appeal Br. 50.) Appellant also argues that "Quane does not teach or suggest the genetic markers or conditions of claim 143, or the first marker in a first gene and a second marker in a second gene of claim 144" (*id.*).

This argument is also unpersuasive. The Examiner has pointed out that AAS discloses BChE (butyrylcholinesterase) mutations that are potentially toxic to patients administered succinylcholine or mivacurium (Answer 5) and Pharmacogenetics discloses polymorphisms of debrisoquine hydroxylase (CYP2D) that affect patient responses to drugs such as codeine (Answer 6). The Examiner relied on these teachings, in combination with the other cited references, as evidence supporting the prima facie case of obviousness (*id.* at 9), and concluded that it would have been obvious to test for the known polymorphisms in these genes and administer anesthesia appropriately based on the results of the genetic testing (*id.* at 10-11).

Therefore, the Examiner did in fact examine the subject matter of claims 143 and 144, and Appellant has provided no basis for concluding that the Examiner erred in concluding that these claims would have been obvious.

II.

The Examiner has rejected claims 151-160, 187, 188, and 190 based on the combination of references discussed above, combined with Lapointe[13]

---

[13] Lapointe et al., US 6,678,669, Jan. 13, 2004.

(Answer 13). The Examiner finds that the previously discussed references do not "specifically teach processing and selecting medical tests using computer programs to predict information" but that Lapointe teaches a computer system that analyzes clinical and biochemical data to generate predictive information (*id.* at 13-14). The Examiner concludes that it would have been obvious to combine Lapointe's neural network with the perioperative screening method made obvious by the other references in order to automate the analysis and enable nontechnical users to understand the results of the genomic data (*id.* at 14). We agree with and adopt the Examiner's findings and conclusion.

Appellant argues that the claims rejected based on the combination of references including Lapointe depend from either claim 149 or claim 189, and are nonobvious for the same reasons that claims 149 and 189 are nonobvious (Appeal Br. 50-51). This argument is not persuasive because we conclude that claims 149 and 189 would have been obvious based on the initial combination of references.

Appellant also argues that the cited combination of references fails to disclose certain elements of dependent claims (Appeal Br. 51; Reply Br. 9). This argument is not persuasive because the Examiner has concluded that the collective disclosures of the cited references would have made obvious the limitations of the rejected claims (Answer 13-14), and Appellant's conclusory argument does not provide an adequate basis for a contrary conclusion. The prior art can make a limitation obvious even if the limitation is not expressly disclosed. *See KSR*, 550 U.S. at 418 ("[T]he analysis need not seek out precise teachings directed to the specific subject

matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.").

Finally, Appellant argues that "there is no motivation to combine the cited references. . . . For example, Lapointe does not teach or suggest characterization of DNA, nucleic acids, genetic testing, perioperative care, or provide any teaching or suggestion to make the Office's combination of references." (Appeal Br. 51.)

This argument is also unpersuasive. As the Examiner has found (Answer 14), Lapointe's disclosure is relevant to the automated diagnosis based on relevant biochemical test data. Lapointe discloses that its neural network system can use biochemical test results as part of the input data (Lapointe, col. 10, ll. 5-19) and can be trained to predict a variety of disease states "based on the identification of factors important in predicting the disease state and combining them with biochemical data" (*id.* at col. 10, ll. 27-29). We agree with the Examiner that Lapointe's disclosure is reasonably related to the disclosures of the other references, and that it would have been obvious to a person of ordinary skill in the art to combine the relevant disclosures.

III.

The Examiner has rejected claim 185 based on the initial combination of references, combined with Lyamichev[14] (Answer 15). The Examiner relies on the previously cited references for the disclosures discussed above,

---

[14] Victor Lyamichev et al., *Polymorphism identification and quantitative detection of genomic DNA by invasive cleavage of oligonucleotide probes,* 17 NATURE BIOTECHNOLOGY, 292-296 (1999).

and concludes that Lyamichev would have made obvious the additional limitation of claim 185 (Answer 15-16). We agree with and adopt the Examiner's findings and conclusion.

Appellant argues that "[c]laim 185 depends upon claim 149, and is non-obvious for at least the same reasons that claim 149 is non-obvious" (Appeal Br. 51). This argument is not persuasive because we conclude that claim 149 would have been obvious based on the initial combination of references.

IV.

The Examiner has rejected claims 125 and 134 based on the initial combination of references and evidence provided by the Specification (Answer 16-17). The Examiner finds that the Specification discloses that each of the genes recited in claims 125 and 134 was known to be "associated with various operative related disorders" (Answer 17) and that Appellant has conceded that "the invention does not claim discovery of newly identified DNA sequences" (*id.*, citing Appellant's response filed March 26, 2001). The Examiner concludes that it would have been obvious to include the recited genes, which were known to be associated with surgical complications, in the method made obvious by the prior art (*id.*). We agree with the Examiner's findings and conclusion.

Appellant argues that claims 125 and 134 depend on claims 106 and 127, respectively, and are nonobvious for the same reasons that claims 106 and 127 are nonobvious (Appeal Br. 52). This argument is not persuasive because we conclude that claims 106 and 127 would have been obvious based on the initial combination of references.

Appellant also argues that the cited references do not suggest using the eleven specific genes recited in the claims (Appeal Br. 52) and that none of the references disclose variants of some of the recited genes (*id.* at 52-53).

These arguments are unpersuasive. The Examiner has pointed to evidence, which Appellant does not dispute, that all of the recited genes were known to have variants that were associated with risk of surgery- or anesthesia-related complications. Thus, including those variants in the perioperative genetic testing method suggested by the prior art would only have required using known elements for their known use; specifically, identifying genetic alleles that were known to be associated with surgical complications in order to avoid those complications. *See KSR*, 550 U.S. at 416 ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."). Appellant has not pointed to any evidence that using the specific combination of genes recited in claims 125 and 134 yields anything more than the predictable result.

SUMMARY

We affirm all of the rejections on appeal.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

lp

CASIMIR JONES, S.C.
2275 DEMING WAY, SUITE 310
MIDDLETON WI 53562